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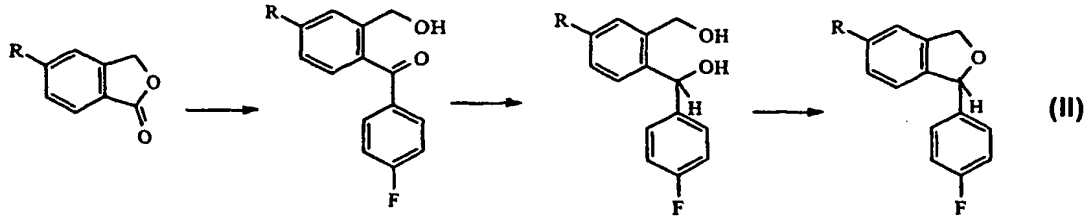
(54) Title: IMPROVED PROCESS FOR THE PREPARATION OF 5-SUBSTITUTED-1-(4-FLUOROPHENYL)-1,3-DIHYDROISOBENZOFURANS



(57) Abstract: The present invention provides a process for the preparation of a 5-substituted-1-(4-fluorophenyl)-1,3-dihydro-isobenzofuran of Formula (2), an intermediate for the manufacture of citalopram, which process comprises: (a) carrying out a Grignard reaction on a corresponding 5-substituted phthalide of Formula (3) in a co-solvent system, comprising adding (i) prepared 4-fluorophenyl magnesium halide in an ether solvent to (ii) the 5-substituted phthalide in a suitable organic co-solvent to the ether solvent, to form a corresponding 4-substituted-2-hydroxymethyl-4'-fluorobenzophenone of Formula (4); (b) carrying out a ketone reduction of the 4-substituted-2-hydroxymethyl-4'-fluorobenzophenone of Formula (4) following the Grignard reaction, to form a corresponding 4-substituted-2-hydroxymethylphenyl- 1-(4-fluorophenyl) methanol of Formula (5); and (c) carrying out a cyclisation reaction on the 4-substituted-2 hydroxymethylphenyl- 1-(4-fluorophenyl) methanol of Formula (5) following the reduction reaction, to form said intermediate of Formula (2); wherein R represents Br or CN.

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